

### Claims

1. A crystal of the ZAP-70 kinase comprising the catalytic domain of ZAP-70 kinase with a unit cell dimension of  $a = 35.77 \pm 5$  Ångstroms,  $b = 57.56 \pm 5$  Ångstroms,  $c = 80.20 \pm 5$  Ångstroms ;  $\alpha = 68.97 \pm 5$  degrees,  $\beta = 89.83 \pm 5$  degrees,  $\gamma = 89.95 \pm 5$  degrees.
2. A crystal of the ZAP-70 kinase comprising the catalytic domain of ZAP-70 kinase wherein said catalytic domain has a three-dimensional structure comprising the atomic structure coordinates of Table 1.
3. A crystal of claims 1 or 2 wherein the catalytic domain of ZAP-70 kinase comprises the sequence of SEQ ID. No. 2, fragment or a homologue thereof.
4. A crystal of claim 3 wherein the catalytic domain of ZAP-70 kinase comprises at least the ATP-binding site.
5. A crystal of any of claims 1-4 bound to at least one ligand or low molecular weight compound.
6. A computer readable medium comprising data storage material encoded with computer readable data wherein said data comprises the atomic coordinates of Table 1 comprising the catalytic domain of ZAP-70 kinase.
7. A method for making a crystal of a ZAP-70 kinase comprising the steps of:
  - (i) purification of the full-length ZAP-70 kinase of SEQ ID No.1
  - (ii) proteolytic domain definition
  - (iii) expression of the full-length ZAP-70 kinase of SEQ ID No.1 flanked by protease recognition sequences to facilitate proteolytic release of the desired domain of ZAP-70
  - (iv) expression of the full-length ZAP-70 kinase of step (iii) in a suitable host cell
  - (v) controlled proteolysis of the desired domain at protease recognition sites
  - (vi) rapid purification of the desired ZAP-70 domain.
8. A method according to Claim 7 wherein the domain comprises the catalytic domain of ZAP-70 kinase of SEQ ID No.2, fragment or a homologue thereof.

9. A method according to Claim 7 and 8 wherein the catalytic domain of ZAP-70, fragment or homologue thereof is bound to at least one ligand or low molecule weight chemical compound at any step prior to crystallisation.

10. A method of determining the three-dimensional structure of the catalytic domain of ZAP-70 comprising:

- (i) crystallisation of ZAP-70 kinase comprising the catalytic domain of ZAP-70 (SEQ ID No.2), fragment or homologue thereof
- (ii) utilizing the atomic coordinates of Table 1 in whole or in part to determine the three-dimensional structure of the catalytic domain of ZAP-70, fragment or homologue thereof.

11. A method for determining the three-dimensional structure of a complex comprising the catalytic domain of ZAP-70 kinase (SEQ ID No.2), fragment or homologue thereof bound to at least one ligand comprising:

- (i) obtaining x-ray diffraction data for crystals of the complex
- (ii) utilizing the atomic coordinates of Table 1 in whole or in part to define the three-dimensional structure of the complex.

12. A method of identifying a ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70 kinase comprising the steps of:

- (i) using the three dimensional structure of the catalytic domain of ZAP-70 kinase derived in whole or in part from the set of atomic coordinates in Table 1 to select a potential ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70
- (ii) selecting those ligands or low molecular weight compounds that bind to the catalytic domain of ZAP-70.

13. A method of identifying a ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70 kinase according to Claim 11 wherein the catalytic domain of ZAP-70 kinase comprises at least the ATP-binding site of said domain.

14. A method of Claims 12-13 for use in selecting ligands which inhibit the biological activity of ZAP-70 kinase.

15. A method of designing a ligand or low molecular weight compound capable of binding to ZAP-70 catalytic domain comprising:

- (i) using the atomic coordinates of Table 1 in whole or in part to determine the three dimensional structure of ZAP-70 catalytic domain
- (ii) probing the said catalytic domain of ZAP-70 with a candidate ligands or low molecular weight compounds to determine which bind to the catalytic domain of ZAP-70
- (iii) selecting those ligands or low molecular weight compounds which bind to the catalytic domain of ZAP-70
- (iv) modifying those ligands or low molecular weight compounds which bind to maximize physical binding properties such as solubility, affinity, specificity or potency.

16. A method according to Claim 15 wherein the candidate ligands or low molecular weight compounds are screened in silico.

17. A method according to Claims 15 –16 for use in designing ligands which inhibit the biological activity of ZAP-70 kinase.

18. A pharmaceutical composition comprising a ligand identified by the methods of Claims 12-14 for use of treatment of diseases and conditions involving T-cell and lymphocyte activation.